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EVALUATION OF PRE-TRANSFUSION LEUKOCYTE COUNT AS A PREDICTOR OF ALLERGIC TRANSFUSION REACTIONS: A RETROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Allergic transfusion reactions (ATRs) are common non-hemolytic adverse events following blood component transfusion. Although donor- and product-related mechanisms have been extensively investigated, recipient-related inflammatory factors are less well characterised. This study evaluated pre-transfusion total leukocyte count (TLC) and absolute neutrophil count (ANC) among patients who developed ATRs.

Methods: This retrospective cohort study included 34 patients who developed ATRs following blood component transfusion between January 2022 and March 2025. Pre-transfusion complete blood count parameters were reviewed, with emphasis on TLC and ANC. Patients were categorised into a leukocytosis group (n=23) and a non-leukocytosis group (n=11) using institutional haematological reference ranges (TLC >10,000/µL and ANC >7,000/µL as elevated values). TLC and ANC were compared between groups using the independent-samples t-test and Mann-Whitney U test. Underlying diagnoses were also stratified.

Results: Of the 34 patients with ATRs, 23 (67.6%) were categorised in the leukocytosis group and 11 (32.4%) in the non-leukocytosis group. Mean TLC was 18,277.8 ± 7,839.4/µL in the leukocytosis group compared with 6,607.5 ± 2,374.6/µL in the non-leukocytosis group. Mean ANC was 13,429.1 ± 6,353.1/µL and 4,025.5 ± 1,698.2/µL, respectively. Both TLC and ANC differed significantly between the groups ($p<0.001$). Diagnostic stratification showed that the leukocytosis group included a broader representation of malignancy, autoimmune, infectious, hepatic, surgical/trauma, and chronic medical conditions.

Conclusion: Elevated pre-transfusion leukocyte and neutrophil counts were frequently observed among patients who experienced ATRs in this cohort. These findings generate a hypothesis that the recipient's pre-transfusion inflammatory state may be relevant to ATR susceptibility. However, because all included patients had already developed an ATR and grouping was based on leukocyte indices, the present study cannot establish leukocytosis as an independent predictor of ATR occurrence. Controlled studies including transfused patients without ATRs are required.

KEYWORDS: allergic transfusion reaction; leukocytosis; neutrophilia; total leukocyte count; absolute neutrophil count; hemovigilance

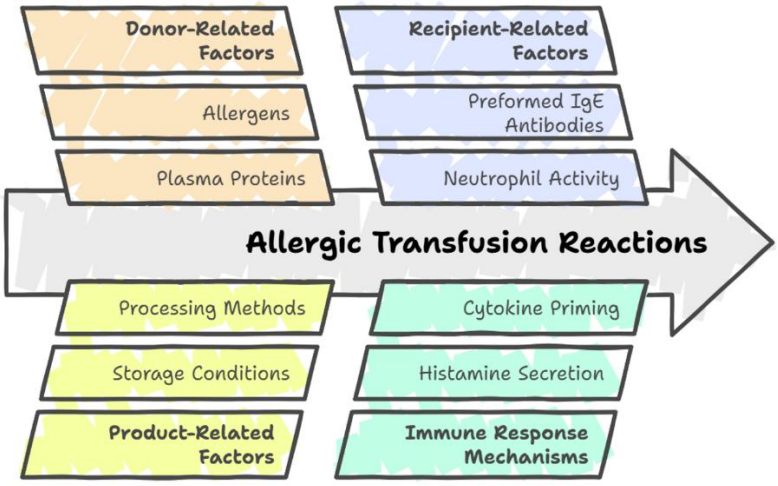
INTRODUCTION

Allergic transfusion reactions (ATRs) constitute an important group of acute non-hemolytic transfusion reactions and occur across different blood components [1,2]. Their clinical manifestations range from localised pruritus and urticaria to erythema, angioedema, bronchospasm, hypotension, and, rarely, severe anaphylaxis [1]. Reported frequencies vary according to the component transfused, surveillance intensity, patient population, and reaction definitions. Platelet and plasma transfusions are particularly associated with ATRs because of their plasma content [1,3].

The pathogenesis of ATRs is heterogeneous. Classical mechanisms involve recipient hypersensitivity to donor plasma constituents, including plasma proteins, with activation of mast cells and basophils and release of mediators such as histamine [1,4]. There are alternative mechanisms that have been proposed: passive transfer of allergens or antibodies and infusion of biologically active mediators that accumulate during component processing and storage [1,5]. These mechanisms do not fully explain why reactions occur sporadically in some recipients or why only a subset of transfusions results in an allergic event.

Evidence increasingly suggests that ATRs may be multifactorial and reflect an interaction between donor, product, and recipient characteristics. Savage et al. emphasised that recipient and donor factors contribute to ATR occurrence and that a minority of recipients may account for a substantial proportion of reactions [6,7]. Nevertheless, recipient-related biological factors remain less well defined than product characteristics such as plasma exposure [5,7].

Figure 1. Schematic representation of various non-transfusion-related factors potentially contributing to allergic transfusion reactions.



Leukocytes, particularly neutrophils, are central components of innate immune and inflammatory responses. In addition to their antimicrobial functions, neutrophils can participate in hypersensitivity pathways through cytokine release, Fc-receptor-mediated activation, and other inflammatory mediators [1,8,9]. Experimental and mechanistic literature has also suggested possible roles for neutrophils and monocytes in allergic responses [1]. This raises the possibility that a pre-existing inflammatory or immune-activated state in a transfusion recipient could influence the clinical expression of an ATR.

Pre-transfusion complete blood count testing is routinely available in many transfused patients. If leukocyte indices are found to have a reproducible relationship with ATR occurrence, they could provide a readily accessible recipient-related marker for future risk-stratification research. The present study therefore evaluated pre-transfusion TLC and ANC among patients who developed ATRs and described the underlying diagnostic spectrum of patients with and without elevated leukocyte indices.

MATERIALS AND METHODS

Study design and setting

A retrospective cohort study was conducted in the transfusion service of a tertiary care teaching hospital. Records of patients who developed an allergic transfusion reaction following blood component transfusion during the period from January 2022 to March 2025 were reviewed.

Study population

The study included 34 patients with documented ATRs for whom relevant pre-transfusion haematological data were available in the study dataset. The analysis was restricted to patients who had developed an ATR; therefore, a non-reaction control group was not included.

Data collection and study variables

Clinical and laboratory information was obtained retrospectively from available transfusion-reaction and patient records. Pre-transfusion complete blood count parameters were reviewed, with particular emphasis on TLC and ANC. The underlying clinical diagnoses were categorised to describe the diagnostic spectrum of the study population. The records from which we obtained our Data also documented reactions following different blood components, including packed red blood cells, platelets, and fresh frozen plasma.

Definition of study groups

The study patients were divided into two groups according to the institutional haematological reference ranges. Group A (leukocytosis group) comprised 23 patients with elevated leukocyte indices, using TLC >10,000/µL and ANC >7,000/µL as the specified elevated values. Group B (non-leukocytosis group) comprised 11 patients without elevation according to these criteria.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 29. Continuous variables were summarized as mean and standard deviation. Differences in TLC and ANC between the two groups were assessed using the independent-samples t-test and Mann-Whitney U test, as performed in the original analysis. A p value <0.05 was considered statistically significant.

Ethical considerations
Ethics approval/waiver details: [Insert Institutional Ethics Committee approval number and date before submission]. As this was a retrospective record-based study, no intervention was performed as part of the study. Patient-identifying information should not be included in the submitted manuscript.

RESULTS

Distribution of study groups
A total of 34 patients with ATRs were included. Of these, 23 (67.6%) were classified in the leukocytosis group and 11 (32.4%) in the non-leukocytosis group.

Table 1. Comparison of pre-transfusion TLC and ANC between study groups

Variable	Leukocytosis group (n=23), Mean ± SD	Non-leukocytosis group (n=11), Mean ± SD	t-test p value	Mann-Whitney U p value
TLC (/µL)	18,277.8 ± 7,839.4	6,607.5 ± 2,374.6	<0.0001	<0.001
ANC (/µL)	13,429.1 ± 6,353.1	4,025.5 ± 1,698.2	<0.0001	<0.001

The mean TLC in the leukocytosis group was 18,277.8 ± 7,839.4/µL compared with 6,607.5 ± 2,374.6/µL in the non-leukocytosis group. Mean ANC was 13,429.1 ± 6,353.1/µL versus 4,025.5 ± 1,698.2/µL, respectively. The differences were statistically significant using both the t-test and Mann-Whitney U test (Table 1).

Diagnostic spectrum
The leukocytosis group included patients with malignant, autoimmune, infectious, hepatic, surgical/trauma, and chronic medical conditions. Malignancies represented in this group included carcinoma of the rectum, head of pancreas, caecum and stomach, chronic myeloid leukaemia, and pleomorphic adenoma. Autoimmune or immune-associated conditions included rheumatoid arthritis, immune thrombocytopenic purpura, rheumatic heart disease, and inflammatory bowel disease. Infectious diagnoses included acute febrile illness, dengue, and typhoid. Surgical and trauma-related diagnoses included Whipple procedure, ruptured ectopic pregnancy, pyeloplasty, inguinal hernia, road traffic accident/head injury, subdural hematoma, and Bartholin cyst. Chronic conditions included anemia, hypothyroidism, and diabetes mellitus. The non-leukocytosis group also included malignancy, infection, surgical/trauma, anemia, hypertension, diabetes mellitus, and coronary artery disease.

Table 2. Diagnostic stratification of the study groups

Diagnostic category	Leukocytosis group (n=23)	Non-leukocytosis group (n=11)
Malignancy	CA rectum; CA head of pancreas; CA caecum; CML; CA stomach; pleomorphic adenoma	CA rectum
Autoimmune/immune-associated	RA; ITP; rheumatic heart disease; IBD	Nil reported
Infection	AFI; dengue; typhoid	Dengue
Liver disease	DCLD/portal hypertension/ascites	–
Surgical/trauma	Whipple procedure; ruptured ectopic pregnancy; pyeloplasty; inguinal hernia; RTA/head injury; SDH; Bartholin cyst	RTA/head injury; ventral hernia
Chronic medical conditions	Anemia; hypothyroidism; diabetes mellitus	Anaemia; hypertension; diabetes mellitus; coronary artery disease

DISCUSSION

In this retrospective cohort of patients who developed ATRs, 67.6% were categorised as having elevated pre-transfusion leukocyte indices, while 32.4% were in the non-leukocytosis group. The leukocytosis group had higher mean TLC and ANC values than the non-leukocytosis group. The diagnostic spectrum of the leukocytosis group also included several conditions associated clinically with inflammation, immune activation, malignancy, infection, tissue injury, or physiological stress.

ATRs are generally understood as heterogeneous hypersensitivity reactions rather than a single mechanistic entity. Plasma proteins and other allergens may interact with recipient antibodies and trigger mast-cell or basophil activation [1,5]. In addition, biologically active mediators present in transfused components may contribute to reactions. Hirayama reviewed both allergen-dependent and allergen-independent pathways and noted that, beyond mast cells and basophils, neutrophils and monocytes may participate in allergic pathways [1]. This provides a biological rationale for exploring recipient leukocyte indices in relation to ATRs. In a randomised controlled trial, Heddle et al. investigated the influence of plasma removal and prestorage leukocyte reduction on acute reactions following platelet transfusion, highlighting the contribution of blood component characteristics to transfusion-related adverse events [10].

Recipient susceptibility is particularly relevant because exposure to a blood component does not uniformly produce an allergic reaction [6,7]. Savage et al. described ATRs as multifactorial events in which donor, product, and recipient factors may all contribute [6]. In a study of platelet transfusions, ATRs were associated more strongly with recipient and donor factors than with several measured product attributes, supporting the concept that characteristics intrinsic to the recipient may influence reaction risk [6]. Similarly, Zheng et al. identified recipient-associated characteristics, including previous ATR history and certain clinical diagnoses, in a paediatric haematology-oncology population, further supporting the importance of recipient-specific factors in ATR occurrence [7]. The present study extends this recipient-focused perspective by examining routinely available pre-transfusion leukocyte parameters.

The predominance of elevated leukocyte indices among affected patients is therefore an observation of potential interest. Neutrophils can release cytokines and other inflammatory mediators and participate in Fc-receptor-dependent immune responses [1,8]. Hosoki et al. described the involvement of neutrophil recruitment in allergic sensitization and inflammation, while Vadas et al. demonstrated an association between platelet-activating factor and the severity of human anaphylaxis [8,9]. A recipient who is already in an inflammatory state may theoretically respond differently to transfused plasma proteins or biologically active mediators. However, the current study did not measure cytokines, IgE, tryptase, basophil activation, or other mechanistic biomarkers. Consequently, an inflammatory mechanism cannot be inferred directly from the leukocyte counts alone.

The underlying diagnostic findings should also be carefully considered. The patients in the leukocytosis group represented had varied primary diagnoses, such as malignancies, infections, autoimmune or immune-associated disorders, hepatic disease, surgery, trauma, and chronic medical conditions. Many of these clinical settings can independently alter TLC and ANC. Therefore, leukocytosis may reflect the underlying illness or physiological stress rather than a specific predisposition to ATR. Future controlled analyses should account for diagnosis, infection, recent surgery or trauma, medications, component type, prior transfusion history, and previous allergic reactions as potential confounders.

An important statistical consideration is that the two study groups were defined using leukocyte indices and were then compared for TLC and ANC. The highly significant between-group p-values are consequently expected and should be interpreted as descriptive confirmation of the group separation rather than evidence that elevated TLC or ANC predicts ATR. Similarly, because every participant in this study had already developed an ATR, the finding that 67.6% had leukocytosis does not establish that patients with leukocytosis have a higher incidence or risk of ATR than transfused patients without leukocytosis.

Despite these limitations, this study has practical value as an exploratory, hypothesis-generating analysis. Pre-transfusion CBC parameters are inexpensive, routinely measured, and readily available. The observed frequency of elevated leukocyte indices among ATR cases provides a basis for a larger analytical study incorporating a control group of transfused patients who do not develop ATRs. Such a design could estimate an odds ratio or relative risk for ATR according to leukocyte status and could use multivariable regression to determine whether TLC or ANC remains independently associated with ATR after adjustment for clinical and transfusion-related factors.

Future work should also examine TLC and ANC as continuous variables rather than relying solely on dichotomous thresholds. Receiver operating characteristic analysis could be considered only in a dataset containing both ATR and non-ATR outcomes. Prospective studies could additionally evaluate inflammatory biomarkers and standardised reaction severity, enabling a clearer assessment of whether recipient inflammatory activation contributes to the pathogenesis or severity of ATRs.

LIMITATIONS

The study has several limitations. First, the sample size was small (n=34) and derived from a single centre. Second, there was no control group of transfused patients without ATRs. Additionally, the unequal sample sizes between the leukocytosis (n=23) and non-leukocytosis (n=11) groups represent an important limitation, potentially affecting statistical power, precision, and the reliability of between-group comparison; therefore, the study cannot estimate the incidence, relative risk, odds ratio, sensitivity, specificity, or predictive value of leukocytosis for ATR occurrence. Third, the groups were defined according to elevated leukocyte indices, making subsequent statistical comparison of TLC and ANC intrinsically dependent on the grouping criterion. Fourth, the retrospective design limited the availability and uniformity of clinical variables. Finally, mechanistic biomarkers of allergic activation were not assessed.

CONCLUSION

In this retrospective cohort, elevated pre-transfusion leukocyte indices were frequently observed among patients who developed allergic transfusion reactions, with 67.6% categorised in the leukocytosis group. The findings support further investigation of recipient inflammatory status as a possible contributor to ATR susceptibility. However, these findings must not be interpreted as demonstrating that leukocytosis independently predicts ATRs. Larger & multi centred studies comparing transfused patients with and without ATRs are required to determine whether pre-transfusion TLC or ANC has independent predictive value.

REFERENCES

1. Hirayama F. Current understanding of allergic transfusion reactions: incidence, pathogenesis, laboratory tests, prevention and treatment. Br J Haematol. 2013;160(4):434-444.
2. Geiger TL, Howard SC. Acetaminophen and diphenhydramine premedication for allergic and febrile nonhemolytic transfusion reactions: good prophylaxis or bad practice? Transfus Med Rev. 2007;21(1):1-12.
3. Tobian AAR, Savage WJ, Tisch DJ, Thoman S, King KE, Ness PM. Prevention of allergic transfusion reactions to platelets and red blood cells through plasma reduction. Transfusion. 2011;51(8):1676-1683.
4. Matsuyama N, Yasui K, Amakishi E, Hayashi T, Kuroishi A, Ishii H, et al. The IgE-dependent pathway in allergic transfusion reactions: involvement of donor blood allergens other than plasma proteins. Int J Hematol. 2015;102(1):93-100.
5. Yasui K, Matsuyama N, Takihara Y, Hirayama F. New insights into allergic transfusion reactions and their causal relationships, pathogenesis, and prevention. Transfusion. 2020;60(7):1590-1601.
6. Savage WJ, Tobian AAR, Fuller AK, Wood RA, King KE, Ness PM. Allergic transfusion reactions to platelets are associated more with recipient and donor factors than with product attributes. Transfusion. 2011;51(8):1716-1722.
7. Zheng Y, Pei D, Sweat L, Ryan M, Mestemacher MA, Gann M, et al. Contribution of donor- and recipient-associated factors to allergic transfusion reactions to platelets. Transfusion. 2021;61(3):744-753.
8. Hosoki K, Itazawa T, Boldogh I, Sur S. Neutrophil recruitment by allergens contribute to allergic sensitisation and allergic inflammation. Curr Opin Allergy Clin Immunol. 2016;16(1):45-50.
9. Vadas P, Gold M, Perelman B, Liss GM, Lack G, Blyth T, et al. Platelet-activating factor, PAF acetylhydrolase, and severe anaphylaxis. N Engl J Med. 2008;358(1):28-35.
10. Heddle NM, Blajchman MA, Meyer RM, Lipton JH, Walker IR, Sher GD, et al. A randomised controlled trial comparing the frequency of acute reactions to plasma-removed platelets and prestorage WBC-reduced platelets. Transfusion. 2002;42(5):556-566.